Remarks

The Office Action dated March 14, 2006 has been carefully reviewed and the following amendments and comments are made in response thereto. By this amendment claims 67, 69-78, 80 and 82-86 are pending. Claims 67, 72-76, 80, 82, 85 and 86 are amended. Claim 68 and 81 are cancelled without prejudice or disclaimer to the subject matter claimed therein. Applicants submit that the amendments to the claims do not introduce any prohibited new matter. Applicants also submit a replacement sequence listing containing sequence identifiers for the sequence disclosed in the specification in Table 3 on page 50. Applicants submit that the replacement sequence listing does not introduce any prohibited new matter. In view of the above amendments and following remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Summary of the Office Action

1. Claims 67 and 68 were objected to as failing to comply with the sequence rules because the amino acid sequence associated with SEQ ID NO: 23 in the claims differs from the amino acid sequence associated with SEQ ID NO: 23 in the sequence listing.
2. The title was objected to for not clearly indicating the invention to which the claims are directed.
3. Claims 67, 72, 82 and 86 were objected to for failing to comply with various formalities.
4. Claims 67-78 and 80-86 were rejected under 35 U.S.C. 112 (first paragraph) for failing to comply with the enablement requirement.
5. Claims 67-78 and 80-86 were rejected under 35 U.S.C. 112 (first paragraph) for failing to comply with the written description requirement.
6. Claims 69-78 and 80-85 were rejected under 35 U.S.C. 112 (second paragraph) for being indefinite.

Compliance with Sequence Rules

The Examiner objected to claims 67 and 68 because both claims allegedly failed to comply with the sequence rules. Specifically, the amino acid sequence of sequence identifier number twenty-three (23) in both claim 67 and 68 differs from the amino acid sequence of sequence identifier number twenty-three (23) originally filed in the specification.

Without acquiescing to the propriety of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have cancelled claim 68, thereby rendering the rejection moot with respect to this claim. Further, Applicants submit that SEQ ID NO: 23 has been removed from

claim 67. Thus, Applicants submit that the objection is rendered moot and Applicants respectfully request withdrawal of the objection to claim 67 and 68 for failing to comply with the sequence rules.

Objections to the Claims

The Examiner objected to the phrase "amino acids residues" in claims 67 and 86 as not being grammatically correct. Without acquiescing to the merits of the Examiner's objection, and solely to expedite prosecution of the instant application, Applicants have amended both claims 67 and 86 to recite "amino acid residues." Therefore, Applicants respectfully request that the objection to claims 67 and 86 be reconsidered and withdrawn.

Additionally, the Examiner objected to claim 72 because the word "confirmation" was allegedly misspelled. Without acquiescing to the merits of the Examiner's objection, and solely to expedite prosecution of the instant application, Applicants have amended claim 72 to replace the word "confirmation" with "conformation." Therefore, Applicants respectfully request that the objection to claim 72 be reconsidered and withdrawn.

Last, the Examiner objected to the phrase "where in" in claim 82 as not being grammatically correct. Without acquiescing to the merits of the Examiner's objection, and solely to expedite prosecution of the instant application, Applicants have amended claim 82 to replace the phrase "where in" with the word "wherein." Therefore, Applicants respectfully request that the objection to claim 82 be reconsidered and withdrawn.

Rejections under 35 U.S.C. 112 (first paragraph)

Claims 67-78 and 80-86 were rejected under 35 U.S.C. 112 (first paragraph) for failing to comply with the enablement requirement. Specifically, the Examiner alleged that instant specification is not enabled for: (1) treating any mammal other than a rat with any peptide sequence and (2) treating rats with other peptide sequences, including those selected from SEQ ID NO: 23-29 or peptide sequences comprising conservative amino acid substitutions. As such, the Examiner purports that the specification is only enabled for methods of treating rats with a peptide consisting of SEQ ID NO: 31. Applicants respectfully traverse the rejection.

Without acquiescing to the propriety of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have cancelled claim 68, thereby rendering the rejection moot with respect to this claim. Further, Applicants have amended claim 67 to be directed towards

peptides of all seven transmembrane domains of a human alpha-1A adrenergic receptor. Support for the amendment is located in the specification on page 22, line 7 to page 23, line 32 and page 50, Table 3.

First, the Examiner stated that the specification does not enable the treatment of hypertension in mammals, other than a rat, with a peptide antagonist to the alpha-1A adrenergic receptor. Specifically, the Examiner states that it is not predictable whether or not treatment of a human with a peptide selected from the rat receptor would result in treatment of hypertension.

Applicants respectfully point out that the amended claims are directed to peptide sequences from the human alpha-1A adrenergic receptor. Importantly, the peptide antagonist, SEQ ID NO: 31, from a rat would provide sufficient guidance to enable the skilled artisan to practice the claimed invention without undue experimentation in any other mammalian system. Given that the amino acid sequences of the transmembrane domains of integral membrane proteins are highly conserved in mammals, those of skill in the art would appreciate that an experimental rat model is routinely used to extrapolate finding to humans. Since, the rat peptide sequence (SEQ ID NO: 31) effectively antagonized the rat alpha-1A adrenergic receptor, it would be expected that a human peptide would similarly antagonize a human alpha-1A adrenergic receptor. Further, Applicants are unaware of any need to treat hypertension in a rat. Rather, the experiments were conducted in a widely accepted rat model of hypertension which has been proven to be indicative of the response in humans. Thus, the specification enables the treatment of hypertension in mammals other than rats.

Second, the Examiner purports it is unpredictable in the art which amino acid sequences selected from an alpha-1A adrenergic receptor transmembrane domain will act as an antagonist of said receptor. Thus, the Examiner reasons that the instant invention is only enabled for the peptide (SEQ ID NO: 31) used in the examples provided in the specification.

According to MPEP 715.07, actual reduction to practice is not required. The specification need not contain a working example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without undue experimentation and the art is not undeveloped and unpredictable (MPEP 2164.02). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (MPEP 2164.01; *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983)). Additionally, an extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance (MPEP 2164.06).

Applicants submit that it would not require undue experimentation for the skilled artisan to use

peptides from all seven transmembrane domains of a human alpha-1A adrenergic receptor to antagonize said receptor. The peptide antagonist, SEQ ID NO: 31, from a rat would provide sufficient guidance from the art, at the time the application was filed, to enable the skilled artisan to practice the claimed invention without undue experimentation. Moreover, Applicants respectfully point out that the skilled artisan has sufficient guidance on how screen peptides of all seven transmembrane domains of an alpha-1A adrenergic receptor for antagonist activity. For example, the peptides may be examined for their ability to inhibit ligand binding by the relevant receptor which has been pre-incubated by the peptide or the peptides may be examined for their ability to impair receptor coupling to second messenger systems.

Further, it is predictable that peptides from all seven transmembrane domains of an alpha-1A adrenergic receptor are able to antagonize said receptor. As indicated by the Examiner, Tarasova *et al.* (J. Biol. Chem. (1999) 274: 34911-34915) ("Tarasova") tested the antagonist properties of peptides prepared from each of the seven transmembrane domains (Tms) of the CXCR4 receptor, which is a GPCR. Tarasova was able to produce peptide antagonists from the second, fourth, sixth and seventh domains of a GPCR (Office Action, page 7). Peptide antagonists from the first, third and fifth transmembrane domain of were not effective because of synthetic difficulties and their poor solubility (Office Action on page 8). Given the high sequence homology among GPCRs, it is predictable that peptides from the second, fourth, sixth and seventh transmembrane domains of the alpha-1A adrenergic receptor (a GPCR) would be effective antagonists.

Moreover, the D2 dopamine receptor (a GPCR) is used in the application as filed as a model for other seven trans-membrane domain receptors (see page 10, line 31 to page 11, line 5). Antagonism of this receptor is shown in the present application to occur using peptides corresponding to fragments of either the VI or the VII domain (see page 37 lines 10 to 22). Moreover, PCT/CA97/00203 further shows that receptor antagonism can be achieved using a peptide corresponding to a fragment of the domain V of the D2 receptor (see page 60, line 9). As such, the evidence has provided that all seven transmembrane region of a GPCR may be antagonized. Therefore, Applicants respectfully submit that the instant specification enables the skilled artisan to use peptides antagonists from all seven transmembrane domains of the alpha-1A adrenergic receptor.

For the reasons stated above, Applicants submit that the instant specification is enabled for treating mammals (not just rats) with a genus of peptides antagonists to the alpha-1A adrenergic receptor. Therefore, Applicants respectfully request that the rejection of claims 67-78 and 80-86 under 35 U.S.C. 112 (first paragraph) for failing to comply with the enablement requirement be withdrawn.

Claims 67-78 and 80-86 were rejected under 35 U.S.C. 112 (first paragraph) for allegedly failing to comply with the written description requirement because the specification only describes a single antagonist peptide comprising a portion of an alpha-1A adrenergic receptor and as such fails to adequately describe the claimed genus of peptide antagonists to an alpha-1A adrenergic receptor. Applicants respectfully traverse the rejection.

Without acquiescing to the propriety of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have cancelled claim 68, thereby rendering the rejection moot with respect to this claim.

Applicants submit that the written description requirement for a claimed genus may be satisfied by the disclosure of relevant identifying characteristics. These representative characteristics of the genus are exemplified by the disclosed species. Applicants have disclosed an antagonist peptide (SEQ ID NO: 31) to an alpha-1A adrenergic receptor. This peptide comprises a transmembrane domain from a GPCR. Since GPCRs are highly conserved, all GPCRs share substantial sequence similarity, including transmembrane domains defined by a stretch of hydrophobic amino acids. As such, Applicants' disclosure of a single species is sufficient disclosure of the entire genus of GPCRs. Therefore, Applicants respectfully request that the rejection of claims 67-78 and 80-86 be reconsidered and withdrawn.

Moreover, claims 67-78 and 81-85 were rejected under 35 U.S.C. 112 (first paragraph) for failing to comply with the written description requirement. Specifically, the Examiner alleged that the specification disclosed peptides comprising 15-20 consecutive amino acids but did not provide guidance directing the skilled artisan to peptides comprising at least 16 amino acids. The Examiner contends that there in no guidance in the specification directing the skilled artisan to peptides comprising at least sixteen amino acids because the genus disclosed in the specification comprising fifteen to twenty amino acids does not provide an adequate written description for peptides comprising more than twenty residues. In support, the Examiner referred to *In re Wertheim*, 541 F. 2d 257, 191 USPQ (CCPA 1976) ("Wertheim") for the holding that a range of 25% to 60% in the specification did not later support a claim limitation of at least 35%. Applicants respectfully traverse the rejection.

Without acquiescing to the propriety of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have cancelled claim 68, thereby rendering the rejection moot with respect to this claim.

Applicants point out that the specification (page 8, lines 20-24) states that, "antagonist peptides

[comprise] amino acid sequences corresponding to at least four, preferably ten and more preferably from fifteen to twenty consecutive amino acids of an integral protein transmembrane domain." Notably, the antagonist peptides may comprise at least four amino acids of a transmembrane domain. This recitation only includes a lower limitation. The mere fact that fifteen to twenty amino acids are preferable is irrelevant. In Wertheim, the new claim limitation which recited "at least 35%" allowed for species to exceed the 65% limitation originally disclosed in the specification. However, Wertheim is inapplicable to instant claim 67 because the specification adequately described antagonist peptides that comprise at least four amino acids of a transmembrane domain. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 67-78 and 81-85 under 35 U.S.C. 112 (first paragraph) for failing to comply with the written description requirement.

Furthermore, claims 67-78 and 81-85 were rejected under 35 U.S.C. 112 (first paragraph) for failing to comply with the written description requirement because the amino acid sequence "GVGVGVFLAAFILMAVAGNLLVILSV" (SEQ ID NO: 23) recited in claims 67 and 68 was not present in the specification as originally filed.

Without acquiescing to the propriety of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have cancelled claim 68, thereby rendering the rejection moot with respect to this claim. Further, Applicants have amended claim 67 to remove sequence identifier twenty-three and its corresponding amino acid sequence. Therefore, the rejection of claims 67-78 and 81-85 under 35 U.S.C. 112 (first paragraph) for failing to comply with the written description is rendered moot and Applicants respectfully request its withdrawal.

Rejections under 35 U.S.C. 112 (second paragraph)

Claims 68 (and claims dependent thereon) was rejected under 35 U.S.C. 112 (second paragraph) as being indefinite. Specifically, the Examiner stated that the claim first recites "a peptide comprising at least sixteen (16) contiguous amino acids" and then later recites "wherein the peptide contains one or more conservative amino acid substitutions in the nine contiguous amino acids." As such, the Examiner alleges that the claim is indefinite because: 1) one cannot determine what is being claimed and 2) the reference to nine contiguous amino acids lacks antecedent basis.

Without acquiescing to the propriety of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have cancelled claim 68, thereby rendering the rejection moot with respect to this claim.

Additionally, claim 80 (and claims dependent thereon) was rejected under 35 U.S.C. 112 (second paragraph) as being indefinite. Specifically, the Examiner alleged that that claims recites a Markush group that only contains one peptide.

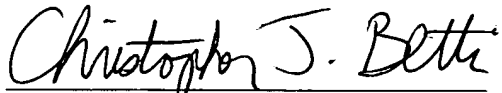
Without acquiescing to the merits of the Examiner's objection, and solely to expedite prosecution of the instant application, Applicants have amended claim 80 such that the claim as amended is directed only to the peptide sequence of SEQ ID NO: 31. Therefore, Applicants respectfully request that the objection to claim 80 (and claims dependent thereon) be reconsidered and withdrawn.

Conclusion

Applicants respectfully request reconsideration of the subject application in view of the substitute claims and the above remarks. It is respectfully submitted that this application is now in condition for allowance. Should the Examiner believe it to be useful, an interview with the Examiner is respectfully requested in order to discuss the foregoing claims.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. 1.136(a)(3).

Respectfully submitted
Morgan, Lewis & Bockius LLP



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Dated: **September 14, 2006**
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